

Remarks

Claims 1-60 are pending in this application. Claims 26-60 have been withdrawn from consideration as drawn to non-elected subject matter. Claims 1-25 are currently under consideration.

I. Response to Rejections under 35 U.S.C. § 103

A. Legal Standards for Examination under Section 103

Before responding directly to the issues raised by the Office Action under Section 103, the legal foundation for sustaining such a rejection will be reviewed. Briefly, an applicant for a patent is entitled to the patent unless the application fails to meet the requirements established by law. 35 U.S.C. §§ 102, 103. It is the USPTO's duty to issue a patent or establish that the applicant is not entitled to a patent under the law. *In re Warner*, 154 USPQ 173, 177 (CCPA 1967), *cert. denied*, 389 U.S. 1057 (1968). Thus, the initial burden is on the USPTO to establish a *prima facie* case of obviousness. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). If no *prima facie* case of obviousness is established, then a rejection under Section 103 cannot properly be sustained. *In re Oetiker*, 24 U.S.P.Q.2d 1443 (Fed. Cir. 1992). If the USPTO establishes a *prima facie* case of obviousness, then the burden of production shifts to the applicant to provide appropriate rebuttal, although the burden of persuasion always remains with the

USPTO. *Id.* Such rebuttal may include arguments, amendments, and/or presentation of objective indicia of nonobviousness. However, such objective indicia are always relevant to a determination of nonobviousness, whether or not a *prima facie* case of obviousness has been established. *Stratoflex Inc. v. Aeroquip Corp.*, 218 U.S.P.Q. 871, 879 (Fed. Cir. 1987). To establish a *prima facie* case of obviousness, the USPTO must show all of the limitations of the claimed invention in the prior art. *In re Ehrreich*, 200 U.S.P.Q. 504, 509-11 (C.C.P.A. 1979). The subject matter of the invention must be considered as a whole and through the eyes of a hypothetical person of ordinary skill, not expert skill, in the relevant art at the time the invention was made. *Connell v. Sears, Roebuck & Co.*, 220 U.S.P.Q. 193, 199 (Fed. Cir. 1983). References must also be considered as a whole, including subject matter that teaches away from the invention as well as subject matter that suggests the invention, and not for their isolated teachings. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 227 U.S.P.Q. 657, 669 (Fed. Cir. 1985). It is not permissible to use hindsight to pick and choose among isolated teachings in the art after first having read Applicant's application to learn the pattern of the invention. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988). Finally, all the

facts in evidence are evaluated, and patentability is determined on the totality of the record. *In re Corkill*, 226 USPQ 1005, 1008 (Fed. Cir. 1985). Factual determinations made by the USPTO must be based on a preponderance of the evidence, and legal conclusions must be correct. *In re Caveny*, 226 USPQ 1, 3 (Fed. Cir. 1985).

Pursuant to established legal authority, patentability under 35 U.S.C. § 103 requires a four-step analysis, which involves determining (1) the scope and content of the prior art, (2) the differences between the prior art and the claimed inventions, (3) the level of skill in the art, and (4) the objective evidence of nonobviousness that may have been presented. *Graham v. John Deere Co.*, 383 U.S. 1, 17, 148 USPQ 459, 467 (1966); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303, 311, 314 (Fed. Cir. 1983). After all of these factors have been considered, the ultimate legal conclusion on the issue of obviousness must be reached. With the above background in mind the rejections under 35 U.S.C. § 103 will be discussed.

B. Factual and Legal Arguments

1. Claims 1-3, 8-9, and 13-24

Claims 1-3, 8-9, and 13-24 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 6,743,436 ("Lee") in view of U.S. Patent No. 6,383,471 ("Chen").

Claim 1 is an independent claim, and claims 2-3, 8-9, and 13-24 are dependent on claim 1.

Lee discloses an anesthetic microemulsion composition for intravenous injection, which contains propofol and a poloxamer, alone or in combination with another co-surfactant. (Col. 4, lines 17-19 and 49-52.) Co-surfactants consist of Solutol HS 15, egg lecithin, Labrasol, polyoxy 10 oleyl ether, Tween, ethanol, and polyethylene glycol. (Col. 4, lines 35-42.)

Chen discloses a pharmaceutical composition including an ionizable hydrophobic therapeutic agent and a carrier. (Col. 2, lines 60-62; Abstr.) The carrier includes an ionizing agent to ionize, and thus solubilize, the therapeutic agent and a surfactant. (Col. 2, lines 62-64; Abstr.) Optionally, the carrier also includes solubilizers, triglycerides, and neutralizing agents. (Col. 2, lines 64-65; Abstr.) The pharmaceutical composition is primarily designed for use in oral dosage forms (Col. 4, lines 62-64; Abstr.), although other dosage forms are not excluded (Col. 35, lines 9-23.) Propofol was included in a long list of ionizable therapeutic agents (Col. 6, line 14, to col. 10, line 35). Ionizing agents are disclosed as pharmaceutically acceptable acids or bases (Col. 11, lines 2-6.) Surfactants are disclosed as hydrophilic, hydrophobic, or a mixture of hydrophilic and hydrophobic surfactants. (Col. 13, lines 62-64.) Specific types

and examples of surfactants are disclosed in long lists at col. 15, line 7, to col. 31, line 25.) Long lists of solubilizers and triglycerides are disclosed, as well. (Col. 31, line 40, to col. 34, line 45.)

The Office Action alleged that it would have been obvious to combine the teachings of Lee and Chen to arrive at the presently claimed invention. Specifically, the Office Action alleged that one would have been motivated to make the combination "in order to formulate an injectable composition that is stable and clear, and with the addition of the tetrahydrofurfuryl alcohol polyethylene glycol ether, provide a maximal concentration of propofol to be administered to a patient."

It is notable that the Office Action states that one would have been motivated to combine the references "in order to formulate an injectable composition that is stable and clear." While Lee is drawn to making an injectable composition, Chen is particularly directed to making an oral formulation. Further, Applicant could find no mention in these cited references of an object to formulate a clear composition or a disclosure of how to formulate a clear injectable composition. Moreover, Applicant respectfully submits the only mention of optical clarity of the presently claimed invention is found in Applicant's disclosure. Still further, the solubilizers of Chen's disclosure are optionally

added to the combination of an ionizable hydrophobic therapeutic agent, an ionizing agent (which is added to solubilize the therapeutic agent by adjusting the pH of the solution to ionize the therapeutic agent; Col. 1, lines 40-43), and a surfactant to "enhance the solubility of the ionizable hydrophobic therapeutic agent in the carrier system (Col. 31, lines 40-43). Therefore, with respect to claim 1, the Office Action alleges that one would be motivated to pick propofol and solutol HS 15 from Lee and to pick tetrahydrofurfuryl alcohol polyethylene glycol ether ("glycofurool") from Chen, while ignoring the requirement for a poloxamer from Lee and the requirement for an ionizing agent and a surfactant from Chen. The Office Action also appears to suggest that one would be motivated to make the necessary combination while ignoring the hundreds of other therapeutic agents, ionizing agents, surfactants, solubilizers, and triglycerides disclosed by Chen. The Office Action further states that one would be motivated to make a clear injectable composition by combining disclosures that do not mention optical clarity. The Office Action still further states that one would be motivated to combine an injectable composition with an oral composition to result in a clear microemulsion-containing composition. Applicant respectfully submits that the motivation to combine these references is absent. It would simply be too hypothetical to pick and choose ingredients,

as proposed in the Office Action, to result in an optically clear composition with a reasonable likelihood of success. Thus, the combination of references is inappropriate, and a *prima facie* case of obviousness has not been established.

With all due respect, although the suggestion to combine references may flow from the nature of the problem, "[d]efining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant to obviousness." *Monarch Knitting Machine Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 880, 4 U.S.P.Q.2d 1977, 1981 (Fed. Cir. 1998). Federal Circuit case law makes clear that the best defense against hindsight-based obviousness analysis is "the rigorous application of the requirement for a showing of a teaching or motivation to combine the prior art references." *Ecolchem Inc. v. Southern California Edison*, 56 U.S.P.Q.2d 1065, 1073 (Fed. Cir. 2000).

As stated in *In re Carroll*, 202 U.S.P.Q. 571, 572 (C.C.P.A. 1979):

One of the more difficult aspects of resolving questions of non-obviousness is the necessity "to guard against slipping into use of hindsight." *Graham v. John Deere Co.*, 383 U.S. 1, 36, 148 USPQ 459, 474 (1965). Many inventions may seem obvious to everyone after they have been made. However, 35 USC 103 instructs us to inquire into whether the claimed invention "would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." Thus, in deciding the issue of obviousness, we must look at the prior art presented from

a vantage point in time prior to when the invention was made, and through the eyes of a hypothetical person of ordinary skill in the art.

Moreover, it has been widely recognized that virtually every invention is a combination of elements and that most, if not all, of these will be found somewhere in an examination of the prior art. This reasoning led the Federal Circuit, in *Connell v. Sears, Roebuck & Co.*, 220 U.S.P.Q. 193, 199 (Fed. Cir. 1983) to state:

The test is whether the claimed invention as a whole, in light of all the teachings of the references in their entireties, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Still further, the Federal Circuit stated as follows:

Obviousness is tested by "what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re Keller*, 642 F.2d 413, 4225, 208 USPQ 871, 881 (CCPA 1981). But it "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." *ACS Hosp. Sys.*, 732 F.2d at 1577, 221 USPQ at 933. And "teachings of references can be combined *only* if there is some suggestion or incentive to do so." *Id.* Here, the prior art contains none.

Instead, the Examiner relies on hindsight in reaching his obviousness determination. But this court has said, "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." *W.L. Gore*, 721 F.2d at 1553, 220 USPQ at 312-13. It is essential that "the decisionmaker forget what he or she has been taught at trial about the claimed invention and cast the mind back

to the time the invention was made . . . to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art." *Id.* One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

In re Fine, 837 F.2d 1071, 5 USPQ2d 1596, 1599-1600 (Fed. Cir. 1988).

Applicant respectfully submits that if one follows the above guidelines and analyzes the art properly, then there is no suggestion of the invention as claimed.

Still further, references must be considered as a whole, including subject matter that teaches away from the invention as well as subject matter that suggests the invention, and not for their isolated teachings. *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 227 U.S.P.Q. 657, 669 (Fed. Cir. 1985). Lee teaches making an injectable composition by combining propofol and a poloxamer. Optionally, a co-surfactant, such as solutol HS 15, can be added to the above mixture. Therefore, Lee teaches away from making a composition that lacks a poloxamer. Further, Chen teaches making an oral composition containing an ionizable hydrophobic therapeutic agent (propofol is one of scores of such agents), an ionizing agent, and a surfactant. Optionally, a solubilizer (glycofurol is one of scores of such solubilizers), a triglyceride, and a neutralizing agent can also be included.

Therefore, Chen teaches away from making a composition that contains glycofurol without also containing an ionizing agent and a surfactant and also ignores the option of adding a triglyceride and a neutralizing agent. Therefore, Applicant respectfully submits that the Office Action did not consider the cited references in their entireties, and the disclosures of the cited references that teach away from making the presently claimed invention were not given due consideration. For these reasons, a *prima facie* case of obviousness has not been established.

Since claims 2-3, 8-9, and 13-24 incorporate by reference the limitations of claim 1 and any intervening claims that may be present, the reasoning set forth above applies to these dependent claims, as well.

For these reasons, withdrawal of the rejections under Section 103 is respectfully requested.

2. Claims 4-7, 10-12, and 25

Claims 4-7, 10-12, and 25 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lee and Chen and further in view of US Patent Application Publication No. 20020107291 ("De Tommaso"). Claims 4-7, 10-12, and 25 are dependent directly or indirectly on claim 1.

De Tommaso discloses an aqueous, clear, injectable pharmaceutical composition including propofol, a pharmaceutically acceptable salt of a bile acid, and lecithin. (§ 0005.) The disclosures of Lee and Chen were described above.

The defects in the *prima facie* case of obviousness against claims 1-3, 8-9, and 13-24 are also present here. The cited references were not considered in their entireties. Also, the cited references were not considered for their disclosures that teach away from making the presently claimed invention. The motivation for combining references is lacking or found only in Applicant's disclosure. Moreover, it is apparent that the conclusions of the Office Action were arrived at using "hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention," *In re Fine*, 5 USPQ2d 1600, *supra*, which is in appropriate procedure for examining claims under accepted Section 103 jurisprudence. For these reasons, a *prima facie* case of obviousness has not been established. Withdrawal of the rejections is thus respectfully requested.

II. Conclusion

Should the Examiner deem it advisable to conduct a telephone interview for any reason, the undersigned attorney would be most

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agreeable to receiving a telephone call to expedite the prosecution of the application.

For the reasons given above, Applicant respectfully requests reconsideration and allowance of Claims 1-25 and passage of this application to issue.

DATED this 16th day of January, 2007.

Respectfully submitted,



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